Urinalysis

I. Specimen collection.

Get a high quality sample -- clean and fresh.
Best time is first urine passed in the morning.

II. Methods.

Voided urine. Clean catch midstream urine.

- · Kneel or squat over a bedpan or stand astride a toilet bowl. Alternatively, sit on the toilet with **the knees spread wide apart**. Reverse seating may help.
- · Gently separate labia minora.
- · Clean urethral meatus from front to back with water or saline -- not soap or disinfectant.
- · Void forcibly, allowing initial stream of urine to pass into the lavatory.
- · **While continuing to void**, collect midstream urine in sterile container.
- · Screw cap firmly on container. Wash hands.
- · Men usually stand. It is important to retract the prepuce if uncircumcised - otherwise same procedure.

Catheter urine.

Unless other methods are impossible or unsatisfactory, don't insert a catheter just to obtain a urine sample.

Suprapubic aspirate.

Very useful in neonates. Also useful in adults if uncontaminated samples can't be obtained and if the question of infection is both in doubt and important.

III. Macroscopic urinalysis.

Solute concentration.

Method of assessment.

Specific gravity (SG) is measured by refractometer. Osmolality measured in the laboratory is much more expensive. Reagent strips for SG are available, but are not very reliable. The urinometer (hydrometer) is no longer used.

Interpretation.

Generally valueless unless you would expect a normal kidney to produce one SG and a diseased kidney to produce another. E.g., in acute oliguria SG rises if the problem is hypovolemia. In acute tubular necrosis, SG stays near 1.010.

To test the kidneys ability to respond to ADH (diagnosing diabetes insipidus and distinguishing central from nephrogenic types), keep the patient strictly without fluid and follow SG. Confirm urine solute concentration by osmometry at the end.

A normal kidney can adjust specific gravity from about 1.001 to 1.030, depending upon the physiologic circumstances. THERE IS NO SUCH THING AS A "NORMAL" SPECIFIC GRAVITY. The relevant question is whether the specific gravity is APPROPRIATE to the patient's current state of salt and water balance.

Every gram per 100 ml of glucose or protein in the urine elevates the specific gravity by 0.003. Radiographic contrast can elevate the specific gravity strikingly.

In very dilute urine pathologic proteinuria or cells may be inconspicuous. As a general rule, "protein in mg/dl should not exceed the last two digits of the SG."

Color.

Red	Blood, hemoglobin, myoglobin, rifampin, and beet
Green, blue	Methylene blue
Yellow	Bilirubin
Bright yellow	Riboflavin

Dipstick Testing

Dipstick semiquantitative chemical tests are used for numerous urinary constituents. They consist of a porous matrix bonded to a paper or plastic strip. Embedded in the porous matrix is a color indicator together with other chemicals that will cause the indicator to change in the presence of various urinary constituents.

pH

Methods.

pH meter -- transport specimen promptly and anaerobically.
Reagent strip. The pH strip is perhaps the simplest dipstick. It merely contains a combination of pH indicator dyes.

Interpretation.

The range that is physiologically possible is from 4.5 to 7.5. There is no "normal" value. The urine pH depends upon what the kidney is called upon to do in regulating acid-base balance and the ability of the kidney to perform that task.

pH is useful in only a few specific circumstances:

In an ammonium chloride urinary acidification test the pH should fall below 5.4.
During infection with a urea-splitting organism pH will rise above 7.
pH may help to check compliance with drug therapy (bicarbonate > 6.5, Mandelamine < 5).

Protein.

Methods.

Dipstick reagent -- relies on the protein error of indicators. Dipsticks are most sensitive to albumin and will miss Bence Jones protein.
SSA (salicylsulfonic acid = sulfosalicylic acid). Used as a confirmatory test. Can be falsely positive with penicillin, radiographic contrast, and some other drugs.
TSA (toluene sulfonic acid) this is sensitive to low molecular weight proteins, including Bence Jones protein.
In the laboratory, specific immunochemical methods are used, particularly for detecting small quantities of albumin. This is important in detecting early diabetic nephropathy.

Glucose.

Dipstick relies on glucose oxidase-peroxidase-orthotolidine. It may be falsely negative with large amounts of vitamin C., with L-dopa, or with tetracyclines. False positive results occur with bleach.

Ketones.

The nitroprusside test detects acetoacetate. It is insensitive to beta hydroxybutyrate. False + with L-dopa, phenolphthalein, and MESNA.

Blood.

Based on peroxidase-like activity of hemoglobin. Sensitivity may be reduced by highly concentrated urine or by ascorbic acid. False positive results can occur from microbial peroxidase in infected urine. The dipstick for blood is more sensitive to myoglobin than to hemoglobin and more sensitive to free hemoglobin than to hemoglobin within erythrocytes.

Nitrite.

Nitrate is normally present in human urine: it can be reduced nitrite by bacteria. This process takes several hours, so the sensitivity for urine infection is around 80% on first morning urines and around 50% on random urines. Not all bacteria convert nitrate to nitrite.

Leukocyte esterase.

This enzyme is present in leukocytes and not much in other cells. This test is reasonably specific for leukocytes in the urine and may help distinguish them from renal tubular cells. It is important to wait the full time recommended.

IV. Microscopy.

Cells.

Erythrocytes.

Indicate bleeding somewhere in the urinary tract or blood added after leaving the body. Dysmorphic red cells (whose most typical feature is blebbing) indicate glomerular disease. Isomorphic erythrocytes mean bleeding below the kidney.

Renal tubular epithelial cells.

RTECs indicate renal damage of a variety of types, both acute and chronic. They do not necessarily indicate primarily tubular disease, although they are often great prominent in some forms of tubular necrosis.
Oval fat bodies are lipid-laden proximal tubular cells. They occur in states of heavy proteinuria, and so are typical of the nephrotic syndrome.

Polymorphonuclear leukocytes.

To be sure that you are dealing with polymorphs you need to see nuclear lobes. Unfortunately, if SG < 1.006, the lobes of the nucleus coalesce into one round nucleus. Leukocyte esterase may confirm leukocyturia. Leukocytes usually denote infection, but they can indicate sterile inflammation, as in lupus nephritis.

Eosinophils.

Eosinophils occur in some but not all forms of acute interstitial nephritis, particularly if induced by antibiotics. When nonsteroidal anti-inflammatory agents cause allergic interstitial nephritis, eosinophiluria is very uncommon.

Lymphocytes.

These are extremely rare but do occur in cases of chyluria and a few cases of transplant rejection. Most "lymphocytes" are actually RTECs.

Bladder epithelium.

Normally a few bladder cells may be found. More are found with cystitis or bladder tumors.

Squamous cells.

> 1 squamous cell/HPF indicates contamination.

Casts.

Erythrocyte casts.

Erythrocyte casts are extremely important finding in the urine. They indicate bleeding from the glomeruli and thus generally a proliferative form of glomerulonephritis or a defect of the glomerular basement membrane, as in inherited forms of nephritis. Blood casts are erythrocyte casts in which the outlines of the cells have been lost, but the golden yellow or orange pigmentation from hemoglobin persists. They have the same significance as erythrocyte casts or low they are more easily confused with other types of casts.

RTEC casts.

These have no specificity for tubular rather than glomerular disease. They just indicate some disease of the kidney.

Leukocyte casts.

These are very readily seen, though often imagined. They indicate either acute pyelonephritis or active inflammatory process in the kidney, such as lupus nephritis.

Granular casts.

Moderate or large numbers indicate some renal disease, but are nonspecific.

Fatty casts.

Fatty casts mean the same as oval fat bodies -- i.e. nephrotic syndrome.

Waxy casts.

Broad waxy casts -- 10 or 12 erythrocytes across, c.f. 3 or 4 for other casts. They are formed in dilated renal tubules and signify chronic renal disease.

Bacteria.

Only rods are visible without stain. >1/HPF in a clean collection likely means UTI.

Crystals.

Cystine crystals -- hexagons -- signify cystinuria. Remember these crystals.
Oxalate crystals occur in ethylene glycol poisoning. A few occur in normal urine.
Urate crystals occur abundantly in acute urate nephropathy (e.g. tumor lysis syndrome). They may also be present in normal acid urine.

Artifacts.

Many strange objects find their way into the urine and cause confusion. Most common are fibers of Kleenex, cotton, talc or other powder, and shards of glass.

V. Automated video microscopy.

Most laboratories now use an automated counting system. Urine poured into the top of the machine splits into three streams. SG is measured by electronically. Dipsticks are read by reflectance color. The third stream passes through a flat chamber and a video microscope films the cells as they whiz by and classifies them. The technologist has a chance to censor any bad calls. The computer then computes the number of cells per "HPF."

Remember: Urine is liquid gold. It is a liquid biopsy obtained without cost or pain to the patient and reflecting pathology within the kidney.

References are available to anyone who is interested.

References.

1. US Preventive Services Task Force. Screening for asymptomatic bacteriuria, hematuria and proteinuria. American Family Physician. 1990; 42:389-395.

2. Woolhandler S, Pels RJ, Bor DH, Himmelstein DU, Lawrence RS. Dipstick urinalysis screening of asymptomatic adults for urinary tract disorders. I. Hematuria and proteinuria. JAMA 1989 Sep 1;262(9):1214-9

3. Corwin HL. "Urinalysis" pp. 295-306 in Schrier RW, Gottschalk CW. Diseases of the Kidney (6th edition). Little Brown and Company, Boston. 1996.

4. Birch DF, Fairley KF, Becker GJ, and Kincaid-Smith P. A. Color Atlas of Urine Microscopy. Chapman and Hall Medical: London. 1994 Pp. 25-57.

5. Risdon P, et al. Which urine sample for detection of proteinuria? Br J Urol. 1989; 63:209-10

6. Bennett PH, Haffner S, Kasiske BL, Keane WF, Mogensen CE, Parving HH, Steffes MW, Striker GE. Screening and management of microalbuminuria in
patients with diabetes mellitus: recommendations to the Scientific Advisory Board of the National Kidney Foundation from an ad hoc committee of the Council on
Diabetes Mellitus of the National Kidney Foundation. Am J Kidney Dis 1995; 25:107-12.

7. Pegoraro A, et al. Simplified screening for microalbuminuria. Ann Intern Med. 1997; 127:817-819.